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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,159	09/21/2006	Larry R. Krepski	C1271.70044US02	5116

23628 7590 11/06/2009

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EXAMINER	
DESAI, RITA J	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
11/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,159	KREPSKI ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-6,8-14,16,20,22,26-28,31,33-36 and 40-70* is/are pending in the application.

4a) Of the above claim(s) *6,9-11,20,22,34,36,59-63 and 66-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5,8,12-14,16,26,28,31,33,37,40-58,64 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/22/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction.

Applicants have elected Group III of the restriction drawn to compounds.

Applicant's election of Group III in the reply filed on 9/21/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The restriction is made FINAL.

Claim Objections

Claims 14-25 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from a multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim 7 is multiply dependent and claims 14 -25 all depend from that is multiply dependent or are multiply dependent and dependent form the claim 7 which itself is multiply dependent.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-5,8,12-14,16,26,28,33,37,40-58,64 and 65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for R2 to an alkoxyalkyl, and

to be a pyrrolidinyl, piperidinyl, morpholine and piperazinyl X to be an alkyl and R1', R" to be a H alkyl or one of them to be a phenyl and the other being a H or an alkyl, and Ra Rb Rc to be H, does not reasonably provide enablement for all the different groups as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds with many different substitutents. The claims reads

Ra' and RI" are independently selected from the group consisting of:
hydrogen,
alkyl,
alkenyl,
aryl,
arylalkylenyl,
heteroaryl,
heteroarylalkylenyl,
heterocyclyl,
heterocyclylalkylenyl, and
alkyl, alkenyl, aryl, arylalkylenyl, heteroaryl, heteroarylalkylenyl,
heterocyclyl, or heterocyclylalkylenyl, substi-tuted by one or more substituents
selected from the group consisting of:

hydroxy,
alkyl,
haloalkyl,
hydroxyalkyl,
alkoxy,
haloalkoxy,
halogen,
cyano,
nitro,
amino,
alkylamino,
dialkylamino,
arylsulfonyl, and
alkylsulfonyl;

A' is selected from the group consisting of: -O-, -C(O)-, $-CH_2-$, $-S(O)_{0-2}-$, and -N(Q-R_4)-;

a and b are independently integers from 1 to 6 with the proviso that a + b is ≤ 7;

R_A and R_B are independently selected from the group consisting of:

hydrogen,
halogen,
alkyl,
alkenyl,
alkoxy,
alkylthio, and
$-N(R_9)_2$;

or R_A and R_B taken together form either a fused aryl ring that is unsubstituted or substituted by one or more R_8 groups, or a fused 5 to 7 membered saturated ring that is unsubstituted or substituted by one or more R_6 groups;

R_a is selected from the group consisting of:

halogen,

alkyl,

haloalkyl,

alkoxy, and

$-N(R_b)_2$;

R_b is selected from the group consisting of:

halogen,

hydroxy,

alkyl,

haloalkyl,

alkoxy, and

$-N(R_b)_2$;

R_c is selected from the group consisting of:

halogen,

hydroxy,

alkyl,

alkenyl,

haloalkyl,

alkoxy,

alkylthio, and

$-N(R_b)_2$;

Q is selected from the group consisting of a bond, $-C(R_d)-$, $-C(R_d)-C(R_d)-$, $-S(O)_2-$, $-C(R_d)-N(R_d)-W-$, $-S(O)_2-N(R_d)-$, $-C(R_d)-O-$, and $-C(R_d)-N(OR_d)-$;

W is selected from the group consisting of a bond, $-C(O)-$, and $-S(O)_2-$;

R_4 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl wherein the alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkyl arylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl groups are unsubstituted or substituted by one or more substituents independently selected from the group consisting of alkyl, alkoxy, hydroxyalkyl, haloalkyl, haloalkoxy, halogen, nitro,

hydroxy, mercapto, cyano, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, amino, alkylamino, dialkylamino, (dialkylamino)alkyleneoxy, and in the case of alkyl, alkenyl, alkynyl, and heterocyclyl, oxo;

R_6 is selected from the group consisting of =O and =S;

R_8 is selected from the group consisting of hydrogen, alkyl, alkoxyalkylenyl, and aryhalkylenyl;

R_9 is selected from the group consisting of hydrogen and alkyl; and

R" is hydrogen or a non-interfering substituent;

with the proviso that when R_A and R_B form a fused heteroaryl or 5 to 7 membered saturated ring containing one heteroatom selected from the group consisting of N and S, wherein the heteroaryl ring is unsubstituted or substituted by one or more R_b groups, and the 5 to 7 membered saturated ring is unsubstituted or substituted by one or more R_c groups, then R_2 can also be -X"-C(O)-N(R_1')(R_1");

2) The nature of the invention: The invention is a (highly) substituted tricyclic compound used to treat viral disorders.

3) The state of the prior art: The state of the prior art is that the drugs and the enzymes react in a lock and key mechanism and the structure of the compound has to be specific. Even a difference of a methyl group verses a hydrogen changes the properties altogether. A good example is a theophylline verses caffeine. They differ by just a methyl group but one of them has a pharmaceutical use as a bronchodilator. There is no absolute predictability and no established correlation between the different substitutions on a core that they would all behave in the exact same way. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

How to Use:-

As stated in the preface to a recent treatise:

"Most non-chemists would probably be horrified if they wereto learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work .....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious) ....." Dorwald F. A.

Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity.

In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. There are no examples with the various substitutents Ra' and RI" are independently selected from the group consisting of:
hydrogen,
alkyl,
alkenyl,
aryl,
arylalkylenyl,
heteroaryl,
heteroarylalkylenyl,
heterocyclyl,
heterocyclylalkylenyl, and
alkyl, alkenyl, aryl, arylalkylenyl, heteroaryl, heteroarylalkylenyl,
heterocyclyl, or heterocyclylalkylenyl, substi-tuted by one or more substituents
selected from the group consisting of:

hydroxy,
alkyl,
haloalkyl,
hydroxyalkyl,
alkoxy,
haloalkoxy,
halogen,
cyano,
nitro,
amino,
alkylamino,
dialkylamino,
arylsulfonyl, and
alkylsulfonyl;

A' is selected from the group consisting of: -O-, -C(O)-, $-CH_2-$, $-S(O)_{0-2}-$, and -N(Q-R_4)-;

a and b are independently integers from 1 to 6 with the proviso that a + b is ≤ 7;

R_A and R_B are independently selected from the group consisting of:

hydrogen,
halogen,
alkyl,
alkenyl,
alkoxy,
alkylthio, and
$-N(R_9)_2$;

or R_A and R_B taken together form either a fused aryl ring that is unsubstituted or substituted by one or more R_8 groups, or a fused 5 to 7 membered saturated ring that is unsubstituted or substituted by one or more R_6 groups;

R_a is selected from the group consisting of:

halogen,

alkyl,

haloalkyl,

alkoxy, and

$-N(R_9)_2$;

R_b is selected from the group consisting of:

halogen,

hydroxy,

alkyl,

haloalkyl,

alkoxy, and

$-N(R_9)_2$;

R_c is selected from the group consisting of:

halogen,

hydroxy,

alkyl,

alkenyl,

haloalkyl,

alkoxy,

alkylthio, and

$-N(R_9)_2$;

Q is selected from the group consisting of a bond, $-C(R_9)-$, $-C(R_9)-C(R_9)-$, $-S(O)_2-$, $-C(R_9)-N(R_9)-W-$, $-S(O)_2-N(R_9)-$, $-C(R_9)-O-$, and $-C(R_9)-N(OR_9)-$;

W is selected from the group consisting of a bond, $-C(O)-$, and $-S(O)_2-$;

R_4 is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkylarylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl wherein the alkyl, alkenyl, alkynyl, aryl, arylalkylenyl, aryloxyalkylenyl, alkyl arylenyl, heteroaryl, heteroarylalkylenyl, heteroaryloxyalkylenyl, alkylheteroarylenyl, and heterocyclyl groups are unsubstituted or substituted by one or more substituents independently selected from the group consisting of alkyl, alkoxy, hydroxyalkyl, haloalkyl, haloalkoxy, halogen, nitro,

hydroxy, mercapto, cyano, aryl, aryloxy, arylalkyleneoxy, heteroaryl, heteroaryloxy, heteroarylalkyleneoxy, heterocyclyl, amino, alkylamino, dialkylamino, (dialkylamino)alkyleneoxy, and in the case of alkyl, alkenyl, alkynyl, and heterocyclyl, oxo;

R_6 is selected from the group consisting of =O and =S;

R_8 is selected from the group consisting of hydrogen, alkyl, alkoxyalkylenyl, and aryhalkylenyl;

R_9 is selected from the group consisting of hydrogen and alkyl; and

R" is hydrogen or a non-interfering substituent;

with the proviso that when R_A and R_B form a fused heteroaryl or 5 to 7 membered saturated ring containing one heteroatom selected from the group consisting of N and S, wherein the heteroaryl ring is unsubstituted or substituted by one or more R_b groups, and the 5 to 7 membered saturated ring is unsubstituted or substituted by one or more R_c groups, then R_5 can also be -X"-C(O)-N(R_1')(R_1");

7) The existence of working examples: The instant specification has examples limited to just a certain scope and substitutent.

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are limited examples, it would be an undue burden and experimentation to make and use.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that,

based on the evidence regarding each of the above factors, the specification, at the time the application was flied, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

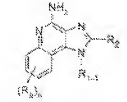
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

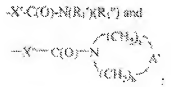
Claims 1-5, 7, 8, 12, 13-33 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 11[1999]-222432. in view of Wermuth et al Bioisosteres.

Applicants claims are drawn to compounds of the formula



IV

wherein R1 -1 is



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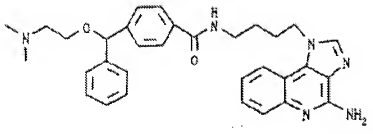
Scope & Content of Prior Art MPEP 2141.01

The prior art teaches the compounds of the formula



(II)

Difference between Prior Art and the claims MPEP 2141.02

The reference has the amides instead of the amines but the activity is the same , strong interferon induction activity.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

Reverse amides are prima facie obvious variations of compounds as they are bioisosters.

See Wermuth

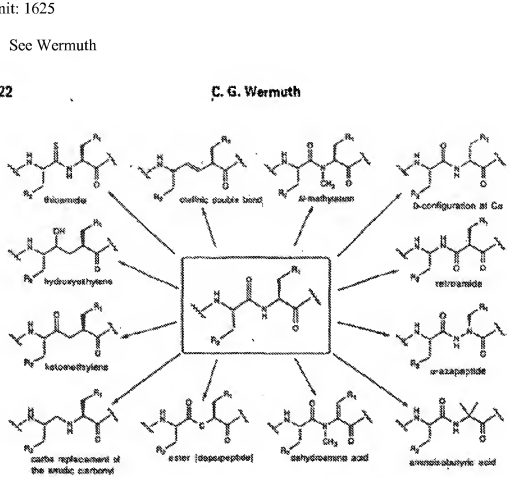
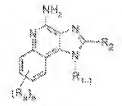


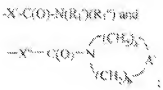
Fig. 13.15 Well-established isosteric replacements for peptidic bonds.[13,14]

Thus bioisoteres are obvious variations to one of skill in the art and hence it would be a prima-facie motivation for one of skill in the art to make such modifications to obtain the compounds of the invention.

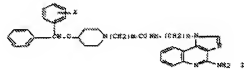
Claims 1-5, 7, 8, 12, 13-33 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 09208584 Nanba Ryoichi et al . 1997 (cited in the IDS.)

Applicants claims are drawn to compounds of the formula



IV wherein R1 -1 is 

Scope & Content of Prior Art MPEP 2141.01



The prior art discloses compounds of the formula

which are again the reverse amides. And the same reasoning as given in view of Wermuth applies.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

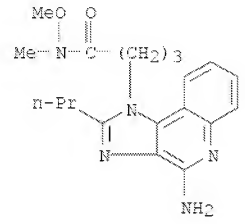
Claims 2 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 2 of copending Application No. 11/595895. Although the conflicting claims are not identical, they are not patentably distinct from each other because The compounds are drawn to the same core with a substitutent which ha N group attached to the X group.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 33 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/883665. Although the conflicting claims are not identical, they are not patentably distinct from each other because the co-pending application is drawn to a pharmaceutical composition comprising the compounds of the invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 33 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/595049. Although the conflicting claims are not identical, they are not patentably distinct from each other because the the co-pending also discloses the pharmaceutical composition which includes the compounds of the invention.



This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Claims *2-5,8,12-14,16,26,28,31,33,37,40-58,64 and 65* are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

November 2nd, 2009.